1- LSS definition

A total of 255 LSS consisting of 1, 2, 3, or 4 concentrations (4 subgroups)

2- Leave one out cross validation for each LSS

a) Form the data subset $Y_{(i)}$ by excluding the profile $i$, $i=1, \ldots, N$

b) Learn: estimate the new model parameters $\text{Pop-PK}_{Y_{(i)}}$ based on $Y_{(i)}$

$c)$ Estimate the individual parameters of the excluded profile $i$ and predict its full PK profile using $\text{Pop-PK}_{Y_{(i)}}$ with its LSS concentrations and covariates

d) Calculate predicted AUC for the profile $i$

e) Validate: calculate the prediction error for the profile $i$

Prediction errors for each LSS

3- Performance evaluation

Estimate error indices for the 255 LSS

Error indices

4- Selection

Select the best LSS of each subgroup in terms of performance and clinical convenience $\Rightarrow$ a total of 14 LSS